

REMARKS

Applicants have received and reviewed the Office Action dated March 26, 2010. Claims 1-11 are pending. Applicants respectfully request reconsideration and withdrawal of the rejections to the pending claims.

Rejections under 35 USC § 103(a)

Claims 1-11 stand rejected as allegedly being obvious under 35 USC § 103(a) in view of Baniel, Raghavarao, Persson, Ullmann, Koch, Stephenson and Davison. Applicants respectfully submit that the present application is not obvious in view of the cited references.

Applicants note that M.P.E.P. 706.02(j) sets forth the standard for a Section 103(a) rejection:

To establish a *prima facie* case of obviousness the prior art reference (or references when combined) **must teach or suggest all the claim limitations**. *In re Royka*, 490 F.2d 981, 985 (CCPA 1974); *see also* MPEP § 2143.03. Additionally, there must be “a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements” in the manner claimed. *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742, 167 L.Ed.2d 705, 75 USLW 4289, 82 U.S.P.Q.2d 1385 (2007). Finally, to establish a *prima facie* case of obviousness there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). Furthermore, the reason that would have prompted the combination and the reasonable expectation of success must be found in the prior art, common knowledge, or the nature of the problem itself, and not based on the Applicant’s disclosure. *DyStar Textilfarben GmbH & Co. Deutschland KG v. C. H. Patrick Co.*, 464 F.3d 1356, 1367 (Fed. Cir. 2006); MPEP § 2144. Underlying the obvious determination is the fact that statutorily prohibited hindsight cannot be used. *KSR*, 127 S.Ct. at 1742; *DyStar*, 464 F.3d at 1367.

A framework for applying the statutory language of §103 is set out in *Graham v. John Deere Co. of Kansas City*, 383 U. S. 1 (1966):

“Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.”

Id. at 17–18.

“[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.”

KSR International Co. v. Teleflex Inc. et al., *supra*, 127 S.Ct. at 1731.

“A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning. *See Graham*, 383 U. S., at 36 (warning against a ‘temptation to read into the prior art the teachings of the invention in issue’ and instructing courts to ‘guard against slipping into the use of hindsight’” (quoting *Monroe Auto Equipment Co. v. Heckethorn Mfg. & Supply Co.*, 332 F. 2d 406, 412 (CA6 1964))).” *KSR International Co. v. Teleflex Inc. et al.*, *supra*, 127 S.Ct. at 1742.

Applicants note that a reference must be considered for everything it teaches by way of technology. *See, EWP Corp v. Reliance Universal Inc.* 755 F.2d 898 (Fed. Cir. 1985). A reference must be considered for all that it taught, disclosures that diverge and teach away from the invention at hand as well as disclosures that point toward and teach the present invention. *In re Dow Chemical*, 837 F.2d 469 (Fed. Cir. 1988). A reference may be said to teach away when a person of ordinary skill in the art, upon reading it, would be discouraged from following a path

set out in the reference, or would be led in a direction divergent from the path taken by the inventor. *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994). Where a reference warns against rather than teaches the invention, one can not be expected to combine it with another teaching. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988). It is error not to give due regard to disclosures in references that teach away. *W.L.Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983).

Applicants submit that none of the references cited either alone or in combination with one another teach or suggest the claims of the present application. Applicants submit that the examination mischaracterizes that which is claimed. Applicants submits that the present invention does not does not involve purification of proteins in the sense that certain desired proteins are separated from other proteins or from organic or inorganic impurity solutes as noted on page 7 of the Office Communication. Instead, the present application involves removal of water from an aqueous protein feed solution in order to concentrate the proteins present in the feed solution. Or more specifically as recited in the claims, “A method for extracting water from an aqueous solution of a protein comprising the steps of: (a) intermixing the aqueous solution of the protein with a sufficient quantity of at least one glycol ether at a temperature at least 30 centigrade degrees above the lower critical solution temperature (LCST) to form a suspension comprising a concentrated aqueous protein phase and a liquid organic phase comprising said at least one glycol ether and at least 10 percent water extracted from the aqueous solution of the protein, wherein the glycol ether has an inverse solubility in water, with the proviso that the solubility of the glycol ether in water is significantly less than the solubility of water in the glycol ether, and the glycol ether does not significantly deactivate the protein, and (b) separating the concentrated aqueous protein phase formed in step (a) from at least a portion of the liquid organic phase.” Applicants further note that there are not any proteins that are separated from other proteins or from impurity solutes. Instead it is only the water that is separated from the proteins present in the feed solution. Furthermore, Applicants have shown that exposure of the feed proteins to the glycol ether does not significantly deactivate these proteins. All of this is new and novel.

Baniel refers to transfer of an organic or an inorganic solute out of one liquid phase (which may be an aqueous phase) into another liquid phase (the solvent phase), or more specifically an aqueous phosphoric acid. Baniel does not involve the transfer of water out of an aqueous feed solution to yield a more concentrated solution as does the presently claimed

application. In fact, Baniel states that the organic solvents must be extracted from the aqueous phosphoric acid.

Furthermore, in the office action, at the top of page 6, it is incorrectly stated that Raghavarao et al. teach two phase extraction methods using glycol ethers.... This is not a correct statement because in fact Raghavarao et al. teach two phase extraction methods using polyethylene glycols and other water-soluble polymers, not glycol ethers. Glycol ethers are not the same as polyethylene glycols. Glycol ethers are low-molecular weight analogs of polyethylene glycols, but are not the same. Their properties are very different, and because of this they are known as a separate class of compounds. In their abstract, Raghavarao et al. teach that the polymers used in a two aqueous extraction are alternatives to "volatile organic compounds as solvents". Glycol ethers are volatile organic compounds (solvents), not polymers. Accordingly, Ragavarao teaches away from the present invention.

Applicants further note that the aqueous two phase extraction as taught by Raghavarao et al. and by Persson et al. is not used to concentrate proteins, but rather to selectively transfer proteins from one aqueous phase (rich in one type of water-soluble polymer or a salt) to another aqueous phase (rich in another type of water-soluble polymer or another salt). Water is present in both phases but water does not transfer between phases.

Additionally, Applicants note that Ullmann et al. do not teach concentration of proteins or another organic solute by extraction of water. Instead, Ullmann et al. teach extraction of an organic solute from an aqueous feed liquid into a second organic liquid (the solvent phase) without forming a stable emulsion. Their example involves extraction of an antibiotic solute out of an aqueous broth into a solvent blend containing acetonitrile and methyl isobutyl ketone (MIBK). Therefore, Ullmann et al. do not concentrate the organic solute by extraction of water.

Finally, Applicants note that Koch teaches a protein concentration method involving precipitation of the protein fraction by heating followed by treating the precipitated protein solids with glycol ethers and water. Unlike the presently claimed invention, this does not involve extraction of water from an aqueous protein solution to produce a more concentrated aqueous protein solution. Precipitation is a difficult process due to the need to handle a precipitated solid phase.

Davison similarly fails to teach or suggest the present invention ether alone or in combination with any other reference as it combines salt, amines and water. Applicants do not

add a second compound such as dextran or a salt to force formation of two liquid phases. Applicants simply heat the glycol ether plus water plus protein mixture to form two liquid phases, one being a water-rich phase that contains the majority of protein at a concentration significantly higher than the concentration of protein in the mixture before phase splitting. The other phase that forms on heating is a glycol-ether rich phase containing water and very little protein. The two phases are created by heating, not by addition of another polymer or salt. The Davison work does not take advantage of a LCST to form two liquid phases, as the present application does.

Accordingly, Applicants submit that the presently claimed application is very different from the prior art for at least the following reasons. Unlike the prior art, Applicants' invention involves transfer of water out of an aqueous protein solution into a glycol ether solvent, without significant deactivation of the protein, in order to concentrate the original aqueous protein solution. All of the proteins entering with the aqueous feed solution remain in the aqueous feed phase, so the purity of the protein fraction is unchanged. Thus, Applicants' invention is not an aqueous protein extraction method as stated by the examiner, but an aqueous protein concentration method. Furthermore, in the examples Applicants illustrated that essentially none of the protein transfers into the glycol ether phase. The glycol ether phase which is produced by contact with the aqueous feed solution (and contains extracted water but not extracted protein) may subsequently be heated to form a second aqueous phase and a water-depleted glycol ether phase, for the purpose of concentrating the glycol ether for recycle back to the process. All proteins stay in the original aqueous feed phase (now concentrated by removal of only water). This is in direct contrast to the cited prior art references because all of the prior art references refer to transfer of an organic or an inorganic solute out of one liquid phase (which may be an aqueous phase) into another liquid phase (the solvent phase), or they require precipitation of the solute. These prior art examples do not involve transfer of water out of an aqueous feed solution to yield a more concentrated solution as recited in the claims of the present application. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 USC § 103(a) rejections to the claims.

Double Patenting Rejections

Applicants note that at the present time the other application has not yet issued. Accordingly, Applicants elect not to address these concerns at this time because they are merely provisional.

CONCLUSION

The Examiner is encouraged to contact the undersigned directly if such contact will expedite the examination and allowance of the pending claims. No additional fees are believed due with this response except as provided, however the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No: 04-1512. If any extension of time or the accompanying response or submission is required, Applicants respectfully request that this be considered a petition therefore.

It is respectfully submitted that this application is in condition for substantive examination, which action is respectfully requested. Any questions that the Examiner may have regarding this correspondence can be directed to the undersigned who may be reached at (317) 337-3848.

Respectfully submitted,

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